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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,154	04/26/2006	Eiichi Kitazono	Q94633	1395

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EXAMINER	
SCHMIDTMANN, BAHAR	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
03/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,154	KITAZONO ET AL.	
	Examiner	Art Unit	
	BAHAR SCHMIDTMANN	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/26/2006;02/15/2007;03/28/2007;12/29/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's Amendment and Remarks filed on 28 October 2009 in which claims 7 and 8 were amended to change the scope and breadth of the claims.

Claims 1-8 are pending in the current application and are examined on the merits herein.

Information Disclosure Statement

The Information Disclosure Statement submitted 29 December 2009 is acknowledged and considered. The Information disclosure statements submitted 26 April 2006, 15 February 2007 and 28 March 2007 are acknowledged and considered.

Objections Withdrawn

Applicant's amendment, filed 28 October 2009, with respect to the objection of claim 7 for failing to further limit the subject matter of the previous claim, has been fully considered and is persuasive because the claim as amended includes limitations that have antecedent basis and further limit the claim from which it depends, i.e. claim 6.

The objection is hereby **withdrawn**.

Rejections Withdrawn

Applicant's amendment, filed 28 October 2009, with respect to the rejections of claim 8 under 35 U.S.C. § 101 because the claimed recitation of a use, without further

setting forth any steps involved in the process, results in an improper definition of a process, has been fully considered and is persuasive because the claim as amended recites an active step of inserting the product into the joint of a patient.

The rejection is hereby **withdrawn**.

Applicant's amendment, filed 28 October 2009, with respect to the rejections of claim 8 under 35 U.S.C. § 112, second paragraph because the claimed recitation of a use, without further setting forth any steps involved in the process, results in an improper definition of a process, has been fully considered and is persuasive because the claim as amended recites an active step of inserting the product into the joint of a patient.

The rejection is hereby **withdrawn**.

Applicant's amendment, filed 28 October 2009, with respect to the rejections of claims 1-7 under 35 U.S.C. §112, second paragraph for indefiniteness, has been fully considered and is persuasive because one having ordinary skill in the art would know that a counter cation is inherently present in the structure whether the counter ion in the form is in the form of a solid salt or an aqueous solution.

The rejection is hereby **withdrawn**.

The following are new ground(s) or modified rejections necessitated by Applicant's amendment, filed on 28 October 2009, where claims 7 and 8 have been

amended to change the scope and breadth of the claims. Therefore, rejections from the previous Office Action, dated 28 May 2009, have been modified and are listed below.

Modified Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsukiyo et al. (US Patent No. 5,733,892, cited in previous Office Action) in view of Shigehisa et al. (JP 06-072893, cited in previous Office Action).

Katsukiyo et al. teaches compounds prepared by linking glycosaminoglycan to phospholipid or lipid (abstract). Examples 4 and 5 provide for the preparation of L-(α-

phosphatidyl)ethanolamine dipalmitoyl-linked glycosaminoglycans (GAG-PPEADP). Specifically, Lot No. 1000 provides for the compound HA1-PPEADP (columns 47-50, tables L and M). Katsukiyo teaches their use as metastasis inhibitors (claim 1).

Katsukiyo et al. teaches the contents of phospholipid or lipid portions in the phospholipid- or lipid-linked glycosaminoglycans represented by formula (VIII) may range from 0.005 to 50% (column 34 lines 40-44). Applicant's disclosure of hydrogel includes the use of 1 to 100 equivalents of phosphatidyl ethanolamine based on 100 equivalents of the carboxyl group of hyaluronic acid (specification, column 6 lines 22-35 and column 7 lines 1-13). The range presented by Katsukiyo et al. is within the range provided in the disclosure.

Katsukiyo et al. also teaches the injectable solutions of the salt forms of the phospholipid- or lipid-linked glycosaminoglycan (column 35, lines 1-3). A syringe containing said injectable solution can be considered as a molded form of hyaluronic acid.

Katsukiyo et al. does not expressly disclose the embodiment of phosphatidyl ethanolamine where the acyl groups are unsaturated.

Shigehisa et al. teaches an antirheumatic compound which uses lipid conjugates of glycosaminoglycans or its salts

Shigehisa et al. teaches that lipid-binding GAG weakens the inflammation of synovial tissue, i.e. the lipid-binding GAG reduces the neoplasia (metastasis) of a synovial cell, fibrin deposition, the coagulation of lymphocytes, as well as prevent the extension of pannus involved in rheumatism (paragraph 0100). Shigehisa et al. teaches

the binding of the carboxylic acid functional group of uronic acid in a glycosaminoglycan with the amine group of a lipid (paragraph 0016, chemical formula 1, C). Shigehisa et al. also teaches that the glycosaminoglycan used can be hyaluronic acid (paragraph 0020) and that the chain length and degree of unsaturation of an acyl group in a lipid are not limited (paragraph 0021). Shigehisa et al. teaches that phospholipid modified GAGs can be administered by intraarticular injection as well as various other forms of administration to the synovial cavity, i.e. joints (paragraphs 0057, 0059, 0066). Shigehisa et al. teaches administering the GAGs to mice (paragraph 0065).

It would have been obvious at the time the invention was made to modify the 6-position of hyaluronic acid with dioleoylphosphatidyl ethanolamine and to administer this compound into the joint of a patient.

MPEP 2141 states, "The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "[R]ejections on obviousness cannot be sustained by mere conclusatory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" KSR, 550 U.S. at, 82 USPQ2d at 1396. Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of

known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) " Obvious to try " choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

Based on the teachings of the MPEP and KSR above, by employing the rationale in (B) simple substitution of one known element for another to obtain predictable results and (G) some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention; one having ordinary skill in the art would have been motivated to modify the 6-position of hyaluronic acid with dioleoylphosphatidyl ethanolamine and to administer this compound into the joint of a patient. Both Katsukiyo et al. and Shigehisa et al. teach that phospholipid modified glycosaminoglycans are useful in inhibiting metastasis. In addition to generally inhibiting metastasis, Shigehisa et al. teaches that phospholipid modified glycosaminoglycans can specifically inhibit metastasis (neoplasia) in the synovial cavity of joints and treat conditions such as rheumatoid arthritis. Therefore, because the

phospholipid modified GAGs taught by Shigehisa et al. is used for similar purpose as that taught by Katsukiyo et al., one having ordinary skill in the art would have been motivated to substite dipalmitoylphosphatidyl ethanolamine for dioleoylphosphatidyl and would predict that this substitution would result in a the instantly claimed compound that should also be suitable for administration into joint.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicant has argued that Katsukiyo et al. teaches that when chondroitin C is reacted with PPEADP the 6^{th} position is substituted, and when hyaluronic acid is used only the terminal aldehyde group is substituted. However, it should be noted that Katsukiyo et al. teaches chondroitin C can be substituted at both the 6^{th} position or the terminal aldehyde group depending on the reaction conditions employed. Furthermore, Shigehisa et al. teaches the same substitution possibilities that can be controlled by using specific reaction conditions set forth in their disclosure. As a result, one having ordinary skill in the art would predict that subjecting hyaluronic acid to the conditions set forth for chondroitin C such that the 6-position is selectively modified with the phospholipid would successfully result in hyaluronic acid modified at the 6-position with said phospholipid.

The rejection is hereby **maintained**.

Conclusion

In view of the rejections to the pending claims set forth above, no claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. BAHAR SCHMIDTMANN whose telephone number is 571-270-1326. The examiner can normally be reached on Mon-Thurs 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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